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PATHOLOGICAL AND EXPERIMENTAL, ON

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[Cincinnati.]
Being a Report to the Board of Health, with an Addendum.

BY ROBERTS BARTHOLOW, M.D.,
Consulting Physician to Mercy Hospital. etc., etc.



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1866.

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BY ROBERTS BARTHOLOMEW, M.D.

Consulting Physician to the Massachusetts General Hospital, &c.

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OBSERVATIONS ON CHOLERA.

Dr. David Judkins, Chairman of the Committee on Mercy Hospital—

SIR.—The closing of Mercy Hospital is a fitting occasion to lay before you some observations made in that hospital upon the excreta, the morbid anatomy, and the treatment of cholera. Facts of this character may be necessary to enable you to complete the history of the epidemic of 1866 as it appeared under your administration of affairs pertaining to the public health.

STATISTICS.—Mercy Hospital was opened on the 16th of August and closed on the 1st of September. During this time fifty-four patients were admitted in the various stages of the disease. The results in the whole number of cases are shown in the following table:

Whole number of cases.....	54
Died.....	25
Per centum of recoveries.....	53.7

The results with regard to the condition of the patients at the time of admission are as follows:

Admitted in Second Stage.....	38
Recoveries.....	20
Admitted in Collapse.....	16
Recoveries.....	1

This table requires a word of explanation. The term "collapse" is used very indefinitely. In the case of recovery from this state, the pulse at the wrist was not absent, but was *very* feeble, and the other phenomena of collapse were well marked.

The mortality as influenced by sex is exhibited in the following table:

Males, cases,	45
Died.....	23
Females, cases,	9
Died.....	2

Of the two deaths amongst the female patients, one was

due to consecutive fever; the other was influenced by the state of pregnancy, in which she was advanced eight months. It is a remarkable fact that in the last named case, beyond a slight dilatation of the os, there was no uterine action.

The influence of age over the mortality is shown in the following table:

Under 12 years of age, cases	3,	died.....	2
From 12 to 20 " " "	8,	"	3
" 20 to 35 " " "	32,	"	6
Above 35 " " "	11,	"	5

According to this table, the danger of a fatal result is greatest under 12; least from 12 to 20; increases from 20 to 35, and again diminishes after 35.

The results in respect to the nationality of the patients, are as follows:

Germans	cases 17,	died.....	9
Irish	" 15,	"	9
Americans	" 18,	"	8
Other nationalities	4.	"	none.

The fifty-four cases terminated as follows:

By death from Collapse.....	20
" " Consecutive Fever.....	6
By recovery.....	28

EXCRETA.—No cases of the *cholera sicca* were admitted. All had the characteristic discharges by stool or vomit, and, with one exception, by both. The gravity of the phenomena appeared to depend to a great extent upon the quantity of the discharge; *ceteris paribus*, those cases proceeded to a fatal termination most rapidly, in which the rice water evacuations were most abundant.

The discharges were alkaline. They consisted of a serous fluid, almost identical with the serum of the blood, columnar epithelium and *debris*. Vibriones were not observed in a single instance.

The urine was suppressed in all cases of collapse, and very scanty in the first and second stages of the disease. A direct ratio existed between the severity of the case and the amount of the urinary secretion. The specific gravity fell with the diminution in the amount, and albumen, epithelium and tube casts appeared early and increased rapidly in quantity. I

have not been able to note the condition of the urine before the accession of cholera symptoms, but the changes in the amount of its normal constituents and the appearance of abnormal ingredients, were manifest in the very inception of the diarrhoeal stage—a fact of importance, equally in a diagnostic and therapeutical point of view.

The perspiration was neutral or feebly alkaline. In the cases of consecutive fever with suppression of urine, a distinct urinous odor was perceived in the sweat.

The alkalinity of the rice water discharges, of the perspiration and the rapid diminution in the acidity and finally, the alkalinity of the urine, are very notable facts in the clinical history of this disease.

MORBID ANATOMY.—No disease presents more uniformity in respect to the morbid anatomy, than cholera. The most obvious phenomena occurring during life—rice water evacuations, suppression of urine, cramps, præcordial anxiety, jerking respiration, collapse, etc.,—are readily explained by structural lesions. Too great importance, therefore, can not be ascribed to the study of the morbid appearances.

It is, perhaps, necessary to describe the methods of investigation pursued, before relating the results. The organs were first examined *in situ*, their position, relations and all those departures from the normal state appreciable by unaided vision, carefully noted. Morbid specimens were examined, first, by a Lawson's binocular microscope, next by an Oberhauser's 1-4 inch and lastly by a Pritchard's 1-7 objective. Sections of the intestine were also studied by a Pritchard's inch objective.

The small intestines were generally well filled with flatus and rice water matter, and were universally injected, minute vessels not ordinarily visible to the naked eye having attained considerable size. The mesenteric vessels were also enlarged. In consequence of this increase of size it was quite possible to trace the distribution of the vessels through the submucous coat and mucous membrane, to the capillary ramification. Remarkable and characteristic alterations were found in the epithelial layer of the mucous membrane. At the earliest

period these alterations consist in a remarkable proliferation of the columnar epithelium and the production of degenerate forms. The villi are matted together by the new matter thus produced, and it adheres with more or less tenacity, all along the intestinal tract. Examined with a power of 300 diameters linear, this matter is seen to be composed of columnar epithelium, lower cell forms, occasionally a villus, and differs from the rice water discharges in containing a much less amount of serum. In many parts of the intestine, especially in the ilium, nothing remains on the basement membrane, but this adhesive matter. After death by consecutive fever, large tracts, of the ilium especially, are found stripped to the basement membrane. There is in either case, nothing intervening between the vessels of the submucous coat, and the contents of the intestine, but the homogeneous, structureless basement membrane—for the cast-off epithelium is excrementitious matter. It is obvious that this destruction of the columnar epithelium, arrests that vital power of selection and transference to the lacteals and veins, possessed by these cells. An outward diffusion current would therefore appear to be inevitable, and hence, the extraordinary congestion of the veins consequent upon the outward flow.

Coincidentally with these alterations in and destruction of, the columnar epithelium, the glandular apparatus of the small intestines, becomes the seat of equally striking changes. The solitary glands enlarge, become filled with a milky fluid and the patches of Peyer thicken. The mesenteric glands also, enlarge somewhat. The solitary glands of the large intestine undergo similar changes. The liver is unaltered, except in the cases of consecutive fever. The gall bladder contains bile in the usual quantity and there is no obstruction to the entrance of it into the intestine; indeed in almost every case bile was found in the small intestine, but unaltered in its physical and chemical characters. These changes in the columnar epithelium and in the glandular apparatus of the intestines, have the effect to arrest, at once and completely, the digestive process, and hence no *fæces* are formed, although bile is present and appears at times in the discharges.

The arrest of the primary assimilation and the rapid loss of

the serum, occasion serious changes in the blood. To study these changes most satisfactorily, it is necessary to compare the blood of the portal vein, just despoiled of many of its constituents by the outward drain through the intestine, and the blood of some remote part of the systemic circulation. The blood becomes viscid, it can not circulate through the lungs to receive oxygen, and the globules, the carriers of oxygen are so damaged as to be unfitted for this function. Hence, the lungs are found after death, comparatively dry, the great venous trunks, the right auricle and ventricle are gorged with blood, and the left cavities are empty and firmly contracted. This change in the fluidity of the blood induces a serious alteration of the red globules, most marked in the blood of the portal veins; they are irregular in outline, many of them are broken up and the serum is crowded with *debris* and granular matter. I have frequently verified the observation that the tenacious matter found in the intestines, restores the arterial color of the blood.

The pleura, sac of pericardium, and peritoneum are coated with a gummy substance which adheres tenaciously to the hands, and so glues the pulmonary and costal pleura together, as to require in some instances, no inconsiderable force to separate them and must have increased the difficulty of respiration. This substance consists of cast off epithelium and the lubricating serum deprived of much of its water.

Early in the disease (death in a few hours after the first symptoms) the kidneys are found dry and bloodless, but this condition soon gives place to a deep congestion, when the pyramids and cortical substance become chocolate colored and microscopical vessels become visible to the naked eye. Subsequently the organs enlarge, the tubes of Ferrein and Bellini become crowded and choked with the cast off epithelium and the Malphigian bodies are gorged with blood. These successive changes correspond with the different stages of Bright's disease, and the rapidity with which they occur, is one of the most remarkable phenomena in the clinical history of cholera.

The cramps, the jerking respiration, and the praecordial

anxiety, find a ready explanation in the condition of the intercranial circulation. The vessels of the base, and of the hemispheres are much distended and their finer ramifications brought into view. The sub-arachnoid spaces are filled with fluid, and the white substance presents on section, numerous bloody points. The particular change most deserving of attentive study, is the marked congestion of the medulla oblongata and pons varolii. On one of the subjects examined, whose case had been particularly characterized by excessive cramps and after death by a remarkable degree of *rigor mortis*, I perceived upon the right thigh a dried matter resembling semen. Carefully moistening it with distilled water I obtained a solution for microscopical examination and ascertained that the dried matter was really semen. This is a striking fact, in confirmation of the view that the cramps are due to reflex action of which the medulla oblongata is the center, or due to the congestion of this organ. This alteration in the circulation of the medulla oblongata and impairment of its nutrition, must affect the electrical relations of its molecules; hence the cramps. As the pneumogastric takes its origin from this center, we have a satisfactory explanation of the jerking respiration and the praecordial anxiety.

In the study of the pathological processes of cholera, we are at once arrested by the changes in the columnar epithelium of the intestinal canal, and the suppression of the renal secretion accompanied, or quickly followed by, extraordinary structural alterations. Which of these lesions is primary?

If the cholera poison is contained in the rice water matter, it probably acts locally upon the intestinal mucous surface and all the other phenomena of the disease are secondary to the changes induced in the blood by the outward diffusion current. It becomes then a matter of prime importance to determine this point. Without designing it I subjected myself to an experimental demonstration.

Experiment I.—A wound upon my left hand, bleeding freely at the time was immersed in the various fluids of the body of a patient in the *post mortem* examination. No result followed.

Experiment II.—A medium sized dog. Some fresh rice water matter was injected subcutaneously and a quantity was thrown into the rectum. Some local inflammation resulted from the injection, but no other effect was produced.

Experiment III.—Same as the preceding, except that considerable rice water matter was also poured into the stomach. Same dog. He continued unaffected.

Experiment IV.—Same dog. Some of the dried matter was made into a solution with water and a portion injected into the thigh and the rest poured into the stomach. In fifteen minutes he had a free watery evacuation which was "frothy," but no other, and no subsequent symptom referable to the ingestion of cholera matter.

As the gastric juice of the dog is powerfully acid and his stomach digestion exceedingly active, it seemed desirable to bring the cholera matter into contact with some other mucous surface.

Experiment V.—Performed tracheotomy on the same dog and injected some cholera matter into the trachea; also, threw some of the same matter into the nasal passages, and poured a quantity into the stomach. Recovered promptly from this rough treatment, ate food, but had no cholera symptoms.

Experiment VI.—Same as the preceding with the same result.

The results of these experiments are, thus far, merely negative. They indicate, however, that the fresh rice water matter and the other fluids of the body in the recent state, are perfectly innocuous. The dried matter appeared to have more effect (*Experiment IV.*) Our future experiments must be made with the rice water discharges in a state of change, if anything may be accomplished in this way. The dejections are poisonous, if at all, under some as yet undetermined condition. I have in contemplation some additional experiments similar in object to those just detailed, and others with the view to ascertain, if possible, the relation of the renal trouble to the other phenomena.

TREATMENT.—The great central facts of the pathological

anatomy of cholera, should be held prominently in view, in the adoption of therapeutical measures. The destruction of the columnar epithelium, the outward diffusion current through the intestinal canal, and the retention in the blood of the poisonous substances eliminated by the kidneys, are the actions to be hindered or prevented by our remedial measures. If these changes pass beyond a certain stage, there are no means known to our art, of arresting them. We can not, by the administration of any remedy, restore the destroyed epithelium, nor pass into the veins a vitalized fluid to supply the place of lost elements, nor cure that condition of the kidney, which the experience of the profession holds to be incurable. In no disease is the *post hoc* more apt to be mistaken for the *propter hoc* than in cholera. The susceptibility to the poison, appears to vary indefinitely. The same plan of treatment is successful in one case and unsuccessful in a precisely analogous one, placed under equally favorable conditions. Great caution is therefore necessary in forming an opinion as to the relative merits of various plans of treatment. Without entering into the *vexata questio* of the best remedy in cholera it will suffice to present the plan, which, based upon the investigations herein detailed, seems most nearly in conformity to the instructions of pathological anatomy. This plan, consists in giving an acid astringent with a diuretic, to promote an inward diffusion current and to excite the functional activity of the kidneys. To prove that this plan is rational, it is only necessary to refer to the alkalinity of the intestinal contents in cholera, and the laws of osmosis as experimentally demonstrated by Graham. The particular prescription employed in accordance with this view was constituted as follows: R Acid Sulphur. Dil. 3ij.; Tinct. Opii Camph. 3vj.; Aqua Camphoræ 3j.; M. S. A teaspoonful every fifteen minutes, half hour, or hour—well diluted.

In this prescription, the benzoic acid of the paregoric elixir was relied on as diuretic. In the stage of collapse or impending collapse, the English army prescription was much employed as the emideas governing the selection of the remedies.

R Ol. Anisi, Ol. Cajeputi, Ol. Juniperi, Acid Hallerii aa 3 s

Ether 3ss; Tinct. Cinnamonia 3j. M. Ten drops every fifteen minutes.

The acid elixir of Haller, consists according to the Prussian pharmacopœia of equal parts of concentrated sulphuric acid and alcohol.

The eliminative plan, so called was pursued in two cases. One in which the symptoms, though violent, were of recent occurrence, produced by a meal of green corn, was cured by castor oil, and the other, the only symptom being violent vomiting of a large quantity of rice water, was cured by ten gr. doses of calomel and injections to open the bowel.

Various other plans of treatment were tried so far as the limited number of cases would admit, but the results were not more satisfactory than before.

My acknowledgements are due to Dr. Geo. S. Courtright, attending physician, for the very intelligent interest manifested by him in all of my researches, and for the aid of his observation and judgement. My thanks are also due to Mr. McCorrick, the apothecary, who rendered valuable assistance in the prosecution of my inquiries.

In conclusion, I beg to present my thanks to the gentlemen of the Board of Health for their confidence in appointing me consulting physician to the cholera hospital, for their liberality in affording every necessary means for the management of the cases, and for the interest manifested by the committee, and especially by its chairman, in everything pertaining to the hospital.

Very respectfully,

ROBERTS BARTHOLOW, M.D.,
Consulting Physician to the Mercy Hospital.

ADDENDUM.

Since I have been engaged in these investigations some researches of Dr. Lionel S. Beale, the distinguished Professor of Pathology in King's College, London, have reached this country in the *Medical Times and Gazette* of August 4th and 18th of the present year. Dr. Beale's published researches are confined to a determination of the changes in the columnar epithelium; he has not thus far extended his inquiry into the excreta; nor does he occupy himself with a study of the

morbid anatomy in general. He promises further important contributions on these subjects.

His researches into the changes occurring in the columnar epithelium have been more elaborate than mine; he has, also studied them with higher powers, and he brings to bear upon these investigations, a facility of manipulation, and an extent of acquirement in the science of microscopy, scarcely equalled by any investigator of our day.

"Those who have made post mortems" says Dr. Beale, "are familiar with the fact that the intestines almost always contain a considerable quantity of pale, almost colorless gruel, or rice, or cream-like matter. This has been proved to consist, almost entirely of columnar epithelium, and in many cases large flakes can be found, consisting of several uninjured epithelial sheaths of the villi. * * * * These important organs, the villi, are in a very bad case, all, or nearly all left bare, and a very essential part of what constitutes the absorbing apparatus is completely destroyed." Dr. Beale has also, studied the changes in the "smaller vessels, and especially in the capillaries and small veins of the villi and sub-mucous tissue. * * * The blood corpuscles appear to have, in great measure been destroyed in the smaller vessels, and in their place are seen clots containing blood coloring matter, minute granules, and small masses of germinal matter, evidently undergoing active multiplication."

The next observation is of exceeding interest in view of that theory which seeks to explain all the phenomena of cholera, by some alteration of the organic nervous system.

"On the other hand, the nerves and ganglia, so numerous between the muscular and mucous coat of the small intestine, exhibit a natural appearance, so that I should not be able to distinguish a ganglia taken from a cholera victim, from one taken from a perfectly healthy person of the same age whose life was destroyed by accident."

In a second paper, Dr. Beale further discusses these changes in the columnar epithelium and gives some engravings of them. He makes a statement in this connection confirmatory of my own observations: "In almost all the cases

of cholera I have yet examined there is evidence of chronic structural change in the *tissues* of the intestine. * * * The columnar epithelial cells often exhibit evidence of chronic change; they seem to be stunted, and in many instances the nuclei are much smaller than in health." In my report, I have alluded to those changes in the columnar epithelium and "the production of degenerate forms." I did not further particularize these changes, but they seemed to me to consist in the first place, in an astonishing proliferation of the columnar epithelium. How, otherwise shall we account for the enormous quantity of cells and debris, which cover in a thick layer the basement membrane, and which in the early stages mat the villi together, and which are discharged in the rice water evacuations? Morbid alterations in the epithelial layer, are, most probably, precedent to the development of cholera symptoms: they are too extensive and important to have been produced in a few hours.

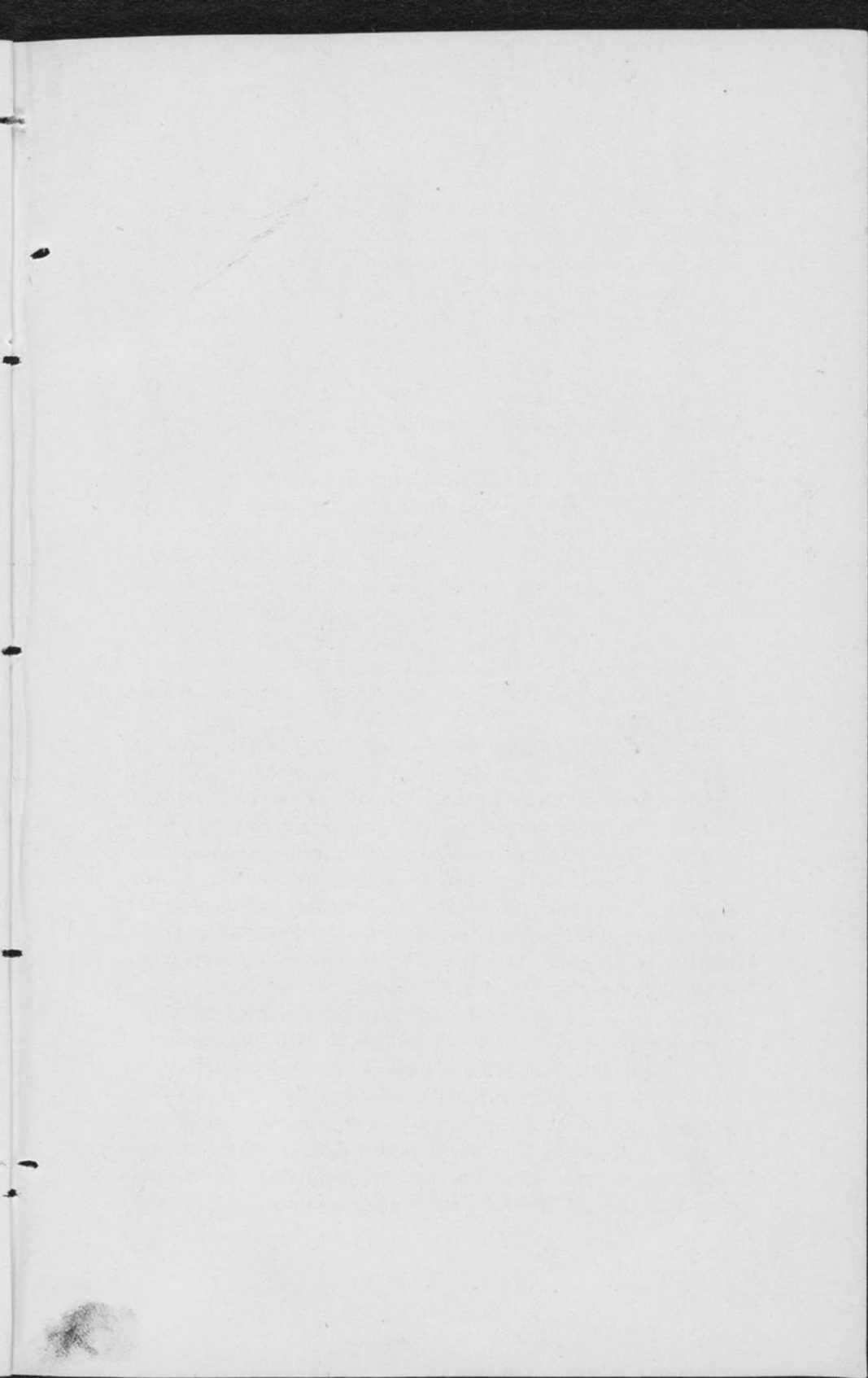
Since my report closed, I have been pursuing the course of experimental investigation therein indicated whenever my leisure permitted. The same dog upon which I had previously experimented has since been subjected to frequent doses of the cholera dejections in a state of decomposition. No other effect has thus far been produced than some slight vomiting and purging. These experiments would seem to indicate that the phenomena of cholera can not be induced in a dog, by the introduction into his organism of the dejections of a cholera patient. Several accidents have apparently demonstrated the innocuousness of this matter when brought into contact with the mucous membrane of the human subject. My friend, Dr. Courtright, who assisted me in these experiments, on one occasion, received some of the decomposing cholera matter in his eye; the same accident happened to myself; more or less of the dried matter was always present in the air of the apartment in which we operated, yet neither had the least symptom of cholera infection. If the poison matter of cholera could be demonstrated to exist in the cholera evacuations, the whole subject would be much simplified. Many of the most obvious symptoms of the cholera

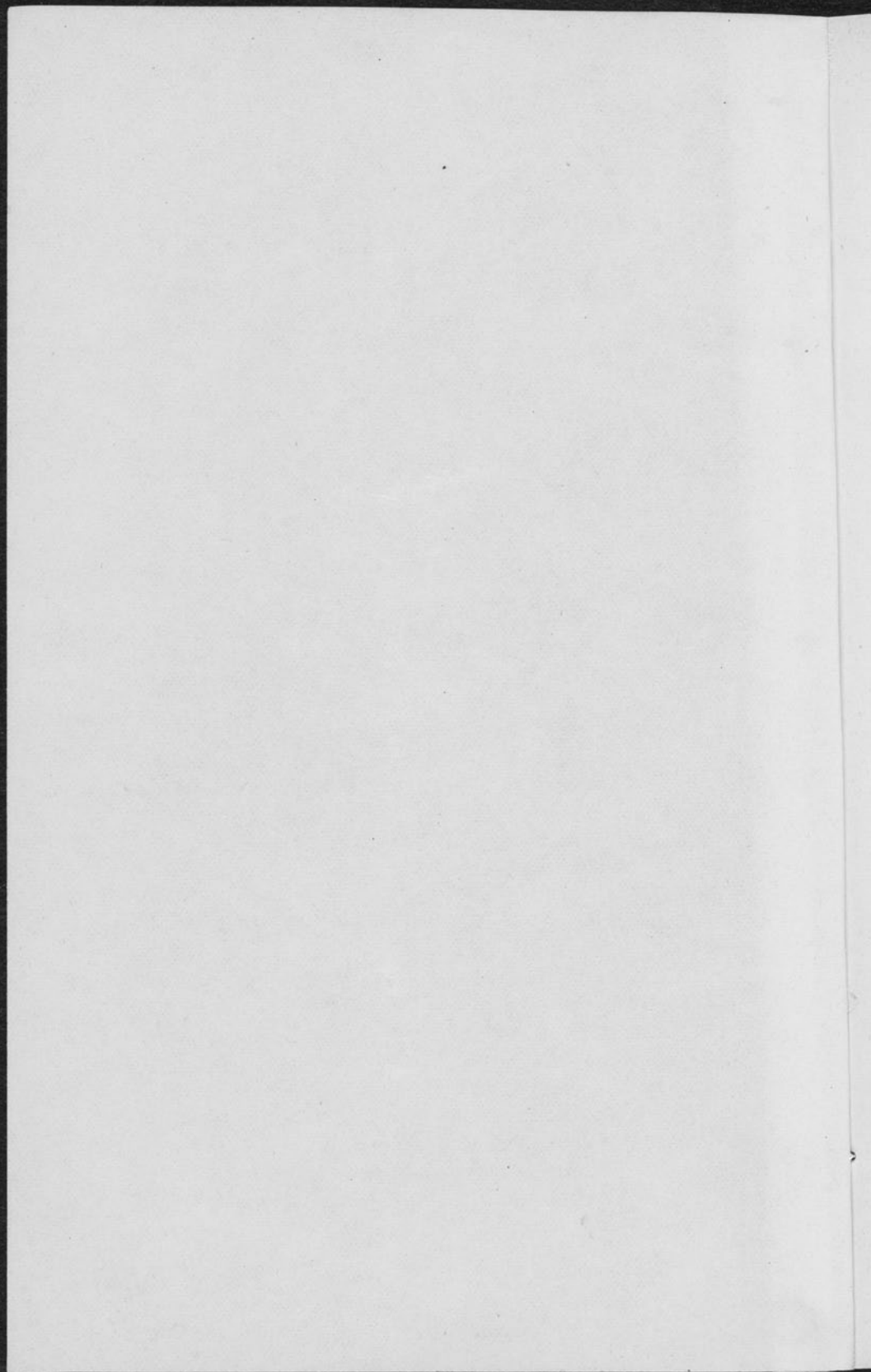
attack can be imitated in animals. Dr. B. W. Richardson (*Medical Times and Gazette*, August 4th,) has proposed an experiment to demonstrate synthetically the following :

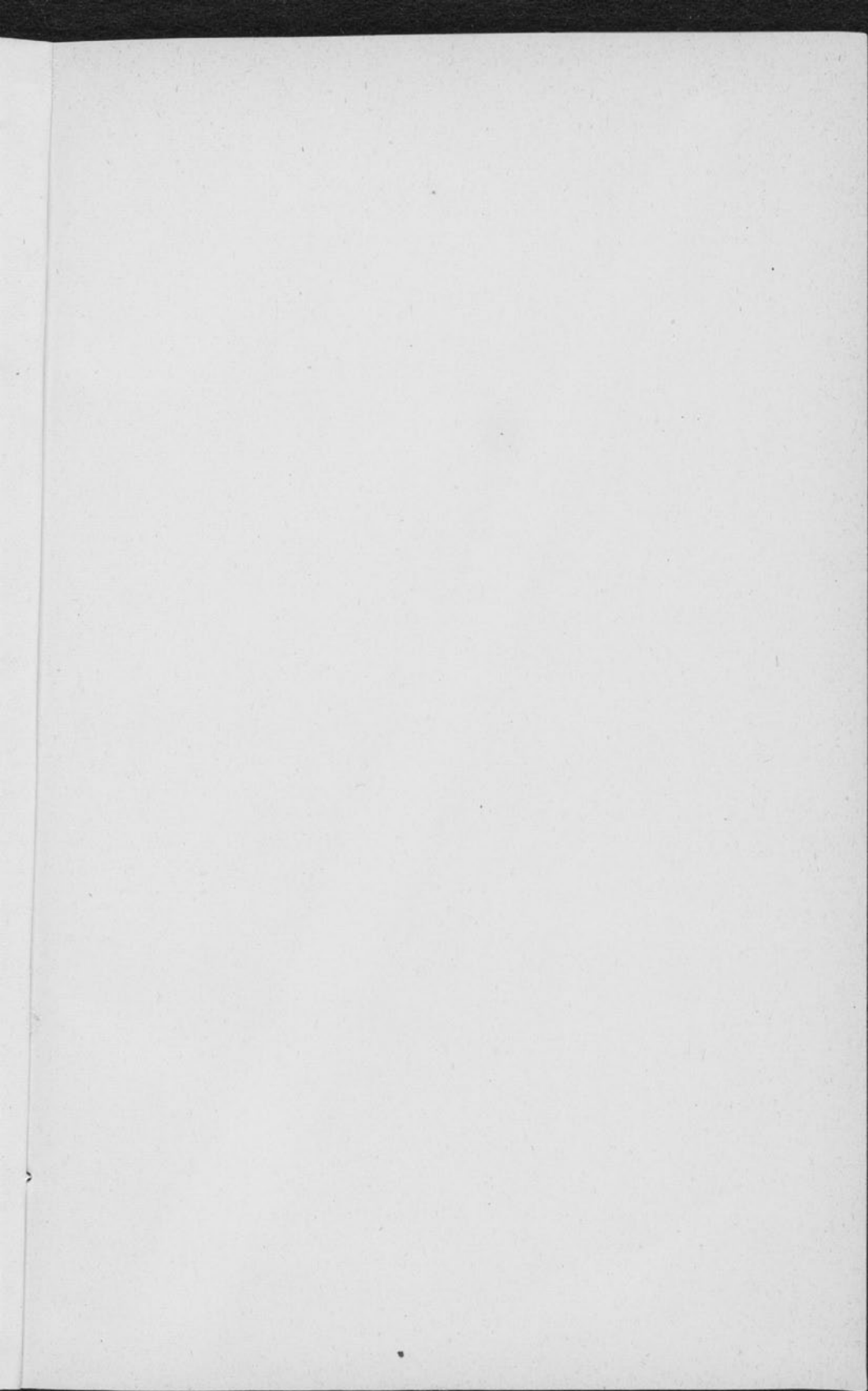
Theorem. *The symptoms of cholera are due to the separation of water from the albumen of the blood and of the tissues.* * * * * If into a serous cavity of an inferior animal, a given quantity of fluid of a specific gravity 100 degrees above that of the animal, be slowly injected there is an immediate transference of watery fluid from the blood to the injected fluid, the osmotic current being especially rapid towards the denser liquid that has been injected. The serous cavity thus fills rapidly with fluid, and if the fluid exuded be drawn off, the flow will be sufficient to cause death by mere loss of water. The symptoms consequent upon this proceeding, are identicle with those of cholera; there is coldness of surface, coldness of breath, convulsive movements, shrinking of tissue and general collapse. After death the morbid conditions found, are the same as those in cholera—viz.: viscosity of the blood, dryness of tissue, and shrunken condition of vascular organs."

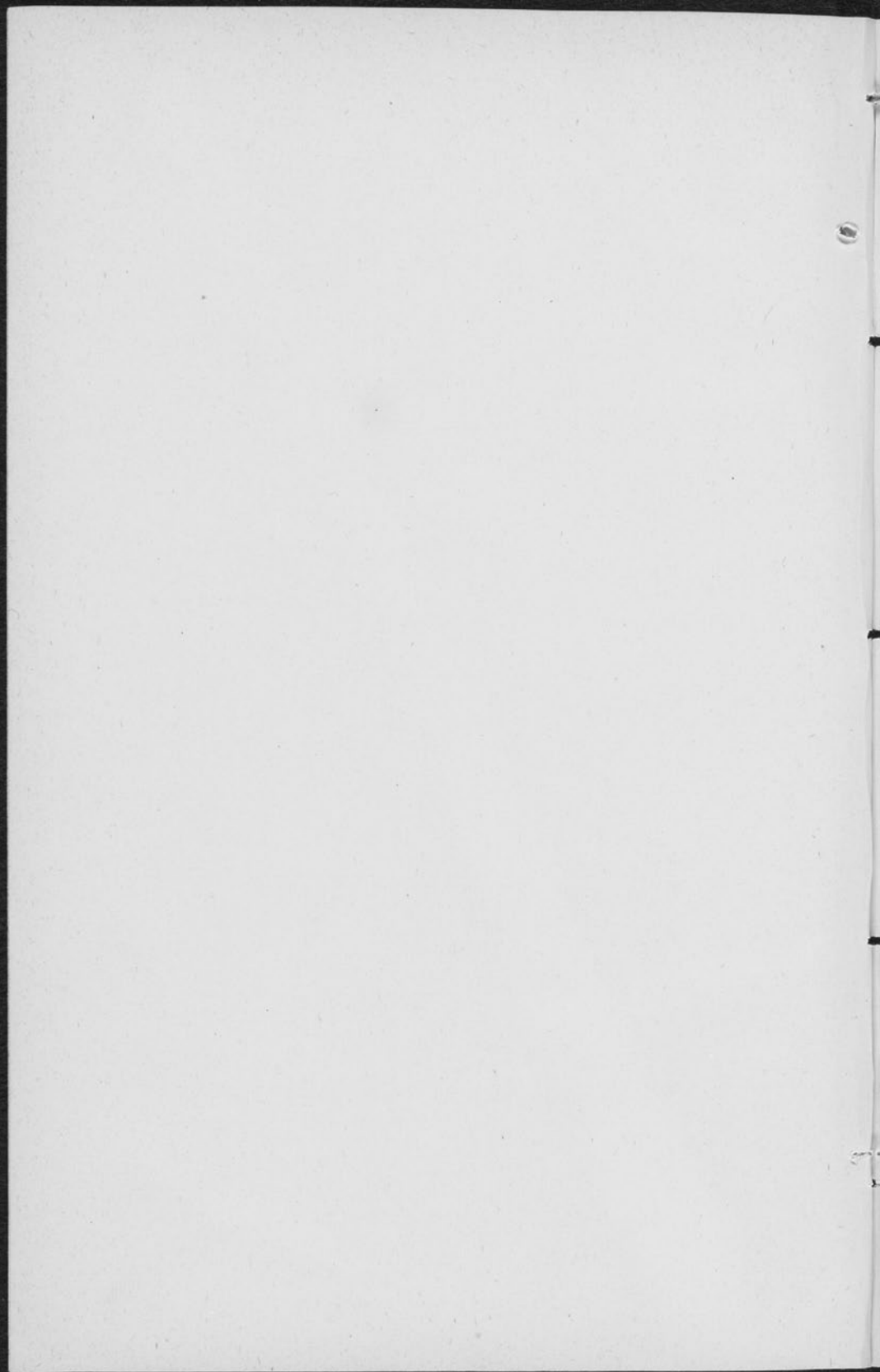
I have repeated these experiments. The animal selected was a young dog. The symptoms produced by injecting a strong saline solution into the peritoneal sac were immediate and striking. The animal lay on the floor in a state of insensibility; an extraordinary pallor of the mucous membrane of the mouth and fauces were observed; the action of the heart was tumultuous and irregular, but there was no decided shrinking and coldness of the surface—the experiment being carried far enough to verify Dr. Richardson's observation, without taking the life of the animal.

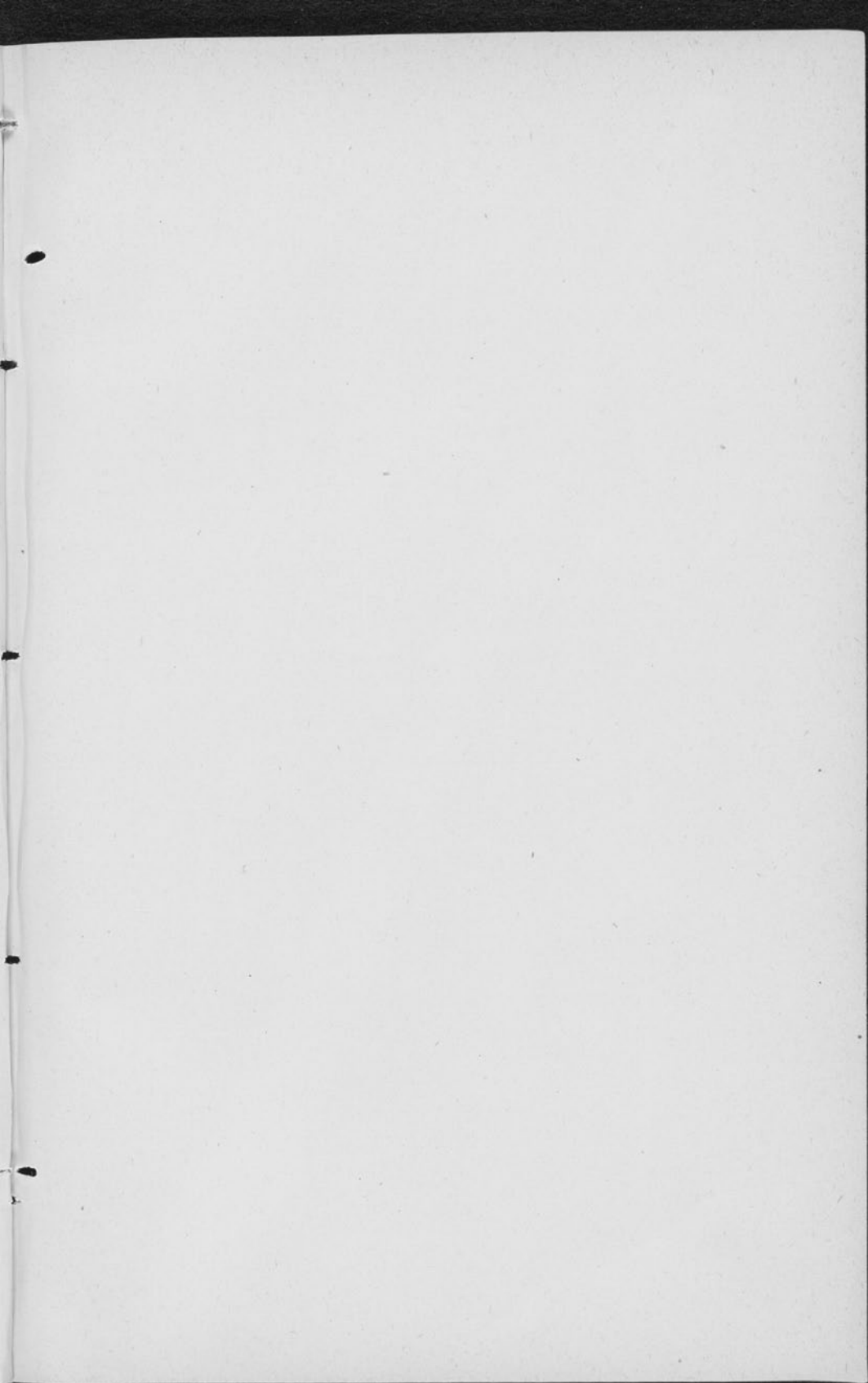
The case of collapse thus artificially induced is a very different affair from the collapse of cholera, in that the important alterations of the epithelial structures, are wholly wanting. If the results of this experiment were identical with the phenomena of cholera, and if the poison of cholera were proved to exist in the dejections, then, indeed, our knowledge of the pathology of this disease would be complete. As the case stands at present, several conditions are wanting.

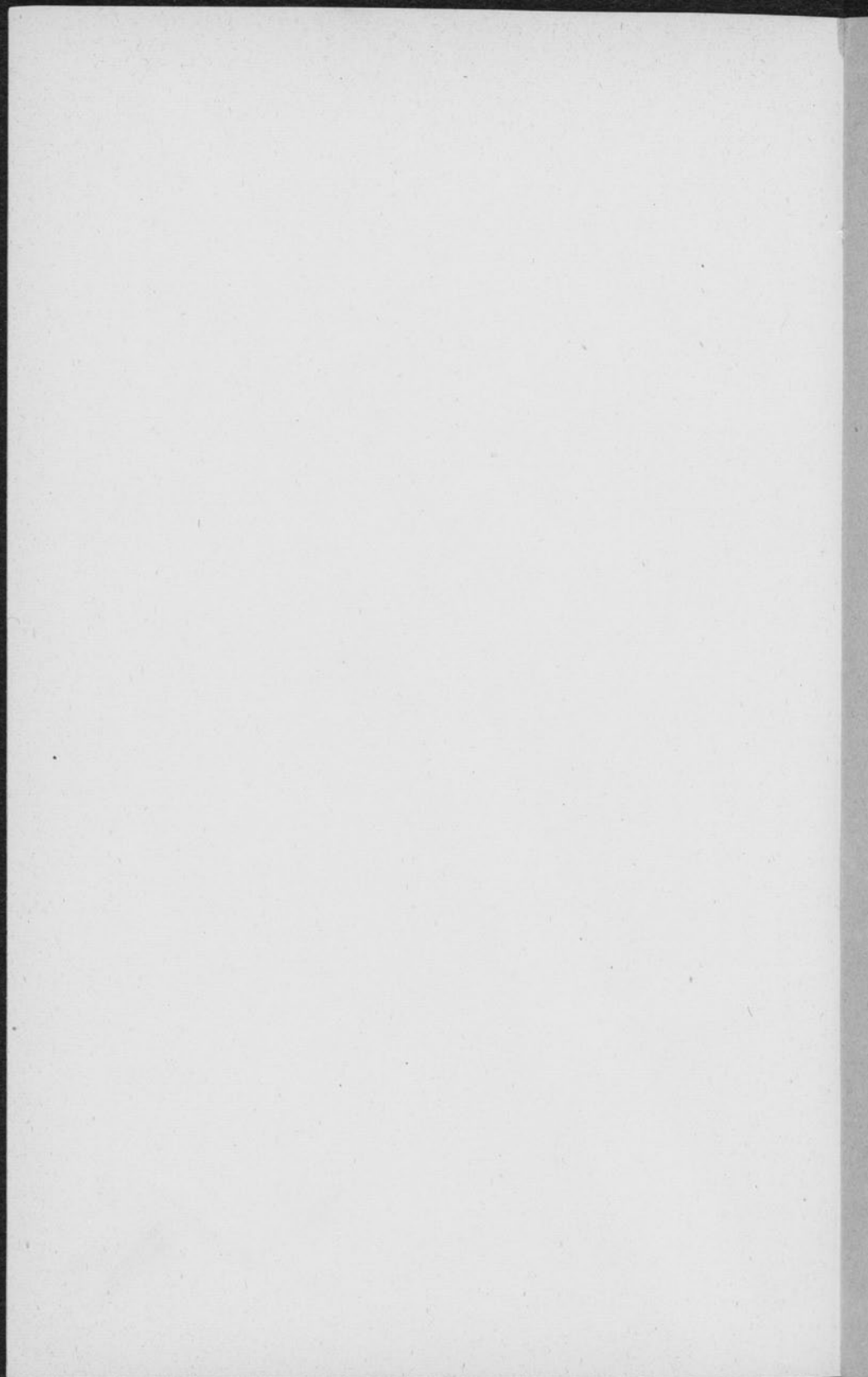


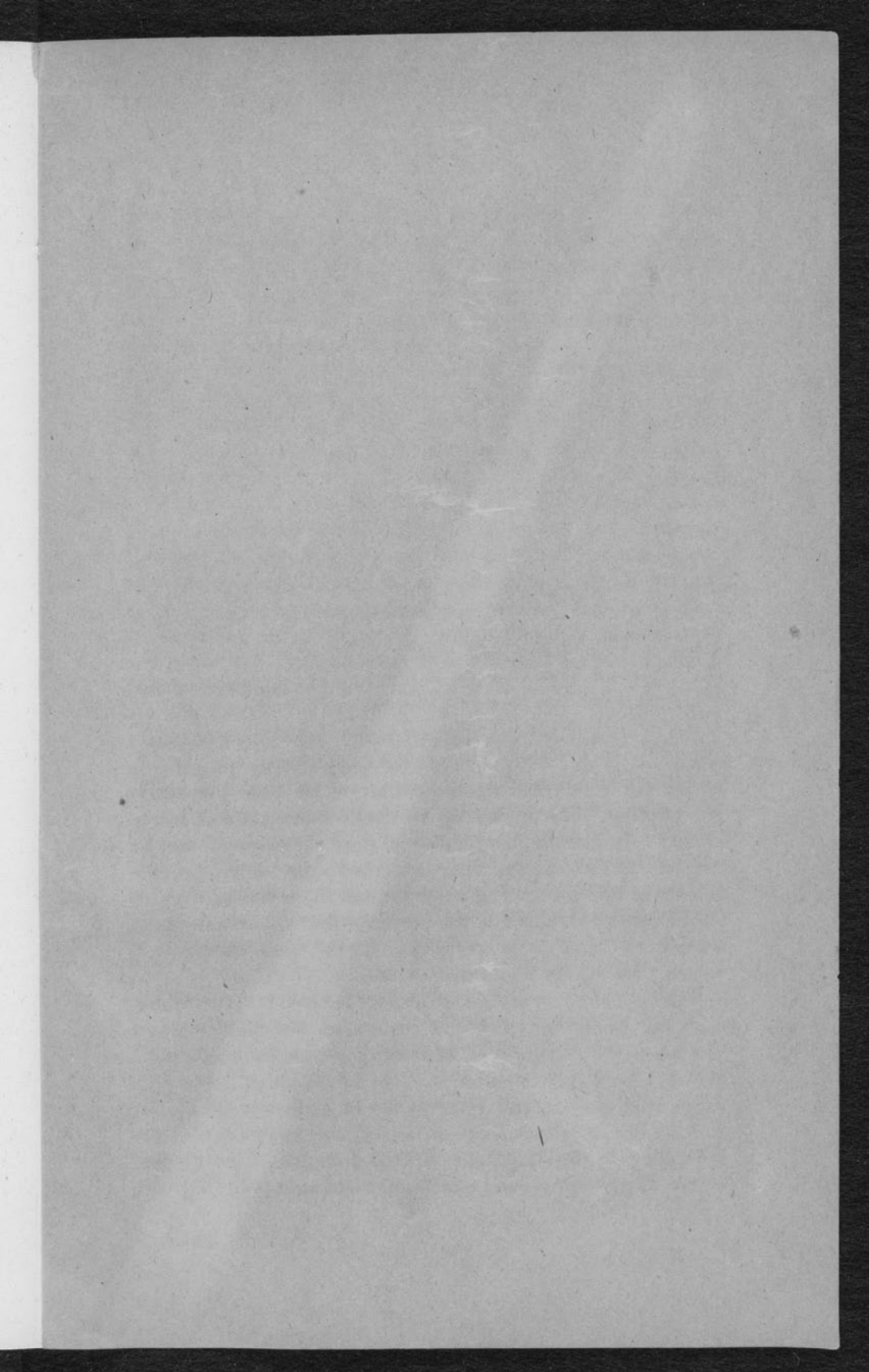












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